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10/799,797	03/12/2004	Jane Ellen Visvader	17496	8972

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EXAMINER	
YAO, LEI	

ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/799,797	VISVADER ET AL.	
	Examiner	Art Unit	
	LEI YAO	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *2, 4, 6, 10-17, 21, 24-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 5, 7-9, 18-20, 22, 23, and 40-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/14/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Response to Amendment and Arguments

The Amendment filed on 4/14/2009 in response to the previous Non-Final Office Action (10/14/2009) is acknowledged and has been entered.

Claims 1-41 are pending.

Claims 2, 4, 6, 10-17, 21, 24-39 have been withdrawn previously for non-elected invention.

Claims 1, 3, 5, 7-9, 18-20, 22, 23, and 40-41, drawn to a method for detecting an aberrant cell or diagnosing the presence of an aberrant cell growth comprising detecting the complex of LMO4- antibody to the extent of monoclonal antibody 16H2 (elected) are under consideration.

The following Office action contains a New Ground of rejection-based on the amendment.

Information Disclosure Statement

The information disclosure statement (s) (IDS) submitted on 4/14/2009 are/is considered by the examiner and initialed copies/copy of the PTO-1449 are/is enclosed.

Rejections/objection Withdrawn

1. The objection of claim 5 because of depending on a withdrawn claim is withdrawn in view of the amendments to the claim.

2. The rejection of claim 18 under 35 U.S.C. 112, 2nd paragraph of insufficient antecedent is withdrawn in view of the amendments to the claim.

3. The rejection of claims 3, 5, 7-9, 18, 22-23, and 41 under 35 U.S.C. 112, scope of enablement- the claims are not enable for claimed method of using mutant or variant

of an antibody to LMO4 containing at least one of the CDRs of the LMO4 antibody is withdrawn in view of the amendments to the claims.

4. The rejections of claim 1, 3, 5, 7-9, 18, 22-23 and 40-41 under 102(b)s are withdrawn in view of amendment of the claims to detect the elevated levels of LMO4 for determining aberrant cell. However, the rejection 19-20 is maintained (see below)

Rejection Maintained and Response to Arguments

Rejection under 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 19 and 20 remain rejected under 35 U.S.C. 102(b) as being anticipated by Kenny et al., (PNAS, vol 95, page 11257-11262, 1998, IDS, Feb 04 2005) as the following:

Claims are drawn to an assay method to detect LMO4 comprising the step of contacting cells in a biological sample with an antibody to L-MO4.

Kenny et al disclose a method of detecting the presence of LMO4 protein with an antibody to LMO4 by forming a complex in the tissue section by immunohistochemistry (page 11257, col 2 and figure 5, page 11260). The tissue section is biological sample containing a cell.

Applicant states the independent claim 1, 3, and 22 have amended to specifically recite a step of comparing the levels of LMO4-immunointeractive molecule complex and determining elevated levels of the complex. The Office agrees with the Applicant, the

rejection of those claims has been withdrawn. The instant claims 19-20 are independent from the claim 1, 3, and 22, and do not recite elevated level of the complex, therefore the rejection of the claims are maintained.

The following is a New Ground of rejection-based on the amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is amended by adding the clause "the level of the *LMO-4 immunointeractive molecule complex in the cells…with the levels of the LMO-4-immunointeractive molecule complex……..and determining the presence of an aberrant cell….. (bridging page 2-3)*. There is insufficient antecedent basis for the limitation of immunointeractive molecule complex in the amended claim because claim 3 is independent claim and drawn to a method comprising contact a cell with LMO4-binding effective amount of an antibody. No immunointeractive molecule has been recited in the previous sentence. Correction is required. See MPEP 2173.05:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 5, 7-9, 18, 22, 23, and 40-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting or diagnosing aberrant epithelial cell comprising ductal epithelial cell in breast, pancreas by elevated levels of LOM4 detected by complex formed with LMO4 and anti-LMO4 antibody or LMO4 and binding molecule BRCA1 compared to normal cells, does not reasonably provide enablement for the method for detecting other aberrant or cancer cells or elevated levels of LMO4 complex formed with other molecules. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to us the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The instant claims are amended to be drawn to a method for detecting or diagnosing an aberrant cell in a subject or in a biological sample from said subject comprising contacting cells or cell extracts from said subject or said biological sample with an immunointeractive molecule specific to LMO4 comprising antibody to LMO4 and determining the aberrant cell by elevated levels of LOM4 complex with the immunointeractive molecule or antibody relative to a normal cell is indicative of an aberrant cell.

To satisfy the requirement of 112, 1st paragraph, it is necessary that the specification provides an enabling disclosure of how to make and use a claimed invention. The objective of the claims is diagnosing or detecting an aberrant cell comprising abnormal growth of cell, cancer, tumor by elevated levels of LOM4. Thus, it would be expected that one of skill in the art would be able to use the method of detecting any aberrant cell comprising cancer, tumor or unwanted proliferation without undue a quantity of experimentations.

The specification teaches LMO4 is developmentally regulated in the mammary gland (example 2, page 64) and is upregulated in primary breast caners detected by immunohistochemistry (example 4, page 66). The specification teaches immunointeractive molecule such as antibody (page 1, line 24). The specification teaches that LMO4 interacts with other its binding molecule BRCA1 etc in breast cancer epithelial cell (example 8-10).

One cannot extrapolate the teachings of the specification to the scope of the claims because 1), the specification does not teach or provide evidence elevated levels

of LMO4 expression in any other cells except breast epithelial cells; 2) The specification although teaches that LMO4 interacts with other proteins, Ldb1, CtIP in normal epithelial and BRCA1 etc in breast epithelial cell (example 8-10), but not showing that the interaction is related with elevated levels of the LMO4 protein in other cancer cells compared to the normal cells; 3) the specification does not provide guideline/direction or predictability showing that the method could be used for detecting or diagnosing any other aberrant cells.

Thus, the examples, the teaching, and the direction/guideline disclosed in the specification are not likely practiced or even predicted for claimed method for detecting any aberrant cell except aberrant epithelial cells; therefore, one of skill in the art would not know how to use the claimed inventions.

LMO4 is a member of Lim domain protein family, function as a transcription factor, and interacts with a binding protein such as Ldb1, LMO seems to be involved in a cell and tissue development such as T cell and gland. LMO4 although has been reported to be overexpressed in the breast cancer epithelial cells as described in the instant specification and Visvader et al (PNAS, vol 98, page 14452-14457, Dec, 2001, IDS filed 2/4/2005, page 6, item 1). Loss or deletion of LMO4 in cancer cells has been reported (Tse et al, Mammalian genome vol 10, page 1089-94, 1999). Particularly, Tse et al teach that LMO4 gene is located in human chromosome Chr 1p22.3 and the chromosome Chr 1p22 has been shown to be deleted in number of human cancers including lymphoma, leukemia, brain, liver, kidney, etc. and LMO4 is expressed in the normal tissues counterparts of all these cancers (page 1092, col 2, last lines). Recent

published article has reported that LMO4 is overexpressed in late stage of pancreas cancer, but the expression is only found in the epithelial origin and limited in the epithelial cell in the cancer tissues (abstract, figures 4-6, and page 2, col 2 of the document. Yu et al, molecular Cancer, vol 7, page 93, Dec 2008). Thus, the state of the art has indicated that the overexpression of LMO4 gene is merely limited to the epithelial cell of the cancer tissues and loss of LMO4 are possible in the cancer cell self.

In view of the lack of sufficient guidance, lack of examples, and lack of predictability associated with regard to the method for detecting aberrant cell by elevated levels of LMO4 assay by more than antibody in the epithelial cell one skilled in the art would be forced into undue a quantitation of experimentations in order to practice the broadly claimed invention.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-6.00pm Monday-Thursday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Lei Yao/
Examiner, Art Unit 1642

/Larry R. Helms/
Supervisory Patent Examiner, Art Unit 1643